Complete Summary

GUIDELINE TITLE

Guidelines for antimicrobial treatment of uncomplicated acute bacterial cystitis and acute pyelonephritis in women.

BIBLIOGRAPHIC SOURCE(S)

Warren JW, Abrutyn E, Hebel JR, Johnson JR, Schaeffer AJ, Stamm WE. Guidelines for antimicrobial treatment of uncomplicated acute bacterial cystitis and acute pyelonephritis in women. Infectious Diseases Society of America (IDSA). Clin Infect Dis 1999 Oct;29(4):745-58. [82 references]

COMPLETE SUMMARY CONTENT

SCOPE

DISEASE/CONDITION(S)

- Uncomplicated acute bacterial cystitis
- Acute pyelonephritis

GUIDELINE CATEGORY

Diagnosis
Treatment

CLINICAL SPECIALTY

Family Practice
Internal Medicine

INTENDED USERS

Advanced Practice Nurses
Physicians

GUIDELINE OBJECTIVE(S)

To provide assistance to clinicians in the diagnosis and treatment of two specific types of urinary tract infections (UTIs) in women:

- Uncomplicated acute, symptomatic bacterial cystitis
- Acute pyelonephritis

Note: The guideline does not address asymptomatic bacteriuria, complicated urinary tract infections, Foley catheter-associated infections, urinary tract infections in men or children, or prostatitis.

TARGET POPULATION

Immunocompetent women

INTERVENTIONS AND PRACTICES CONSIDERED

Antimicrobial therapy

- Trimethoprim-sulfamethoxazole
- Trimethoprim alone
- Trimethoprim and ofloxacin
- Fluoroquinolones, such as norfloxacin, ciprofloxacin, and fleroxacin (oral or parenteral)
- Beta lactams
- Nitrofurantoin or fosfomycin
- Amoxicillin or amoxicillin/clavulanic acid
- Ampicillin/sulbactam with or without aminoglycoside

MAJOR OUTCOMES CONSIDERED

Primary outcome

- Eradication of initial bacteriuria, which was assessed at the follow-up visit closest to 7 days after the end of therapy.

Secondary outcomes

- Recurrent bacteriuria (defined as documentation of eradication of the initial infecting bacteria followed by a new episode of bacteriuria within 6 weeks after the end of therapy)
- Adverse effects (defined as all new symptoms or signs, not just those thought by the investigators to be "probably related" to the antimicrobials)

METHODOLOGY

METHODS USED TO COLLECT/SELECT EVIDENCE

Hand-searches of Published Literature (Primary Sources)
Hand-searches of Published Literature (Secondary Sources)
Searches of Electronic Databases

DESCRIPTION OF METHODS USED TO COLLECT/SELECT THE EVIDENCE

Two separate reviews and analyses were done, one for cystitis and one for pyelonephritis. For each, the review began with a Medline search making use of key words such as "cystitis," "urinary tract infection," "UTI," "acute pyelonephritis," and "kidney infection." These articles were supplemented with others obtained from their bibliographies and from reviews, monographs, and textbooks. Only articles in English could be reliably reviewed.

Acute uncomplicated bacterial cystitis

Studies reviewed included studies of women with acute bacterial cystitis, which was characterized as dysuria, frequency, and/or urgency confirmed by the presence of bacteriuria in adult nonpregnant women with apparently normal urinary tracts. Articles were excluded if they did not include a clinical description of the urinary tract infection or the patient population and if it was not possible to remove from the analysis: pregnant patients, those who were less than 12 years of age, or those with complicated urinary tract infections (urinary catheterization, renal transplantation, or urologic abnormalities). Articles were also excluded if greater than 2% of patients had fever and/or flank pain or asymptomatic bacteriuria or were men. Also excluded were studies of urinary tract infections in selected patient groups with a specific medical illness, such as diabetes mellitus. Inclusion criteria required the article to state that all patients had "cystitis," "uncomplicated urinary tract infection," or one or more of dysuria, frequency, and urgency; were "women," "adult females," or females greater than or equal to 12 years of age; had a quantitative urine culture yielding greater than or equal to 10^2 cfu of a uropathogen/mL; were assigned to oral antimicrobial regimens by prospective randomization; and had at least one follow-up visit for microbiological assessment after antimicrobial therapy.

Of the several thousand titles and abstracts screened, 337 articles were identified that possibly met inclusion criteria and were copied and reviewed by two reviewers. Of these, 76 indeed did meet exclusion and inclusion criteria for the analysis. Of the 76, 53 used $\geq 10^5$ cfu/mL as the quantitative break point for diagnosis of bacteriuria, 11 used $\geq 10^4$, 3 used $\geq 10^3$, 8 used $\geq 10^2$, and 1 accepted any organisms found by suprapubic aspiration of bladder urine. Some used lower concentrations for diagnosis of urinary tract infection caused by Staphylococcus saprophyticus than for that caused by Escherichia coli. All were randomized, as required by inclusion criteria, and 32 were double-blinded. Fifty-five trials did not exclude from analysis patients infected with organisms resistant to one or more of the trial antimicrobials.

Not all of the 76 articles meeting the criteria were used because of inappropriate comparators or insufficient power and/or because they were not amenable to meta-analysis.

Acute uncomplicated pyelonephritis

Except for flank pain and/or fever, exclusion criteria were similar to those used for acute cystitis. Inclusion criteria required statements that each patient had "acute pyelonephritis," "kidney infection," "febrile urinary tract infection," or flank pain (and/or tenderness) and/or fever. Patients had to be "women," "adult females," or females greater than or equal to 15 years of age and had to have at least one follow-up visit after antimicrobial therapy for microbiological assessment. Because of the dearth of papers anticipated in this category, two differences from the cystitis inclusion criteria were that bacteriologic documentation, although required, was not required to be quantitative, and randomized antimicrobial assignment was not required for initial review.

Studies of antimicrobial treatment of acute uncomplicated pyelonephritis that met our criteria were uncommon. Of several hundred articles screened by title and abstract, only 42 appeared relevant, and of these, only nine met our inclusion and exclusion criteria. Of these nine, five were prospective, randomized, controlled trials. However, one randomized patients to two durations of therapy and used a variety of antimicrobial regimens. Thus, only four randomized, controlled trials of antimicrobial agents could be adequately reviewed.

NUMBER OF SOURCE DOCUMENTS

Acute uncomplicated bacterial cystitis

- 76 articles met the inclusion criteria

Acute uncomplicated pyelonephritis

- 4 randomized controlled trials

METHODS USED TO ASSESS THE QUALITY AND STRENGTH OF THE EVIDENCE

Weighting According to a Rating Scheme (Scheme Given)

RATING SCHEME FOR THE STRENGTH OF THE EVIDENCE

Grades reflecting the quality of evidence on which recommendations are based:

I. Evidence from at least one properly randomized, controlled trial
II. Evidence from at least one well-designed clinical trial without randomization, from cohort or case-controlled analytic studies (preferably from more than one center), from multiple time-series studies, or from dramatic results of uncontrolled experiments
III. Evidence from opinions of respected authorities based on clinical experience, descriptive studies, or reports of expert committees

METHODS USED TO ANALYZE THE EVIDENCE

Meta-Analysis
Systematic Review with Evidence Tables

DESCRIPTION OF THE METHODS USED TO ANALYZE THE EVIDENCE

Two authors read each article in English that appeared to meet a priori inclusion and exclusion criteria and completed a data form for each article. All authors reviewed articles meeting inclusion and exclusion criteria, and pertinent data were sorted into tables. Prospective, randomized, controlled trials were accepted for analysis and assessed individually, if of sufficient size. Trials of comparable agents were consolidated by use of meta-analytic techniques.

Statistics. The relative effect of one antimicrobial compared with that of another was estimated by the risk difference: the difference in the observed probabilities of end point events. For meta-analyses of multiple studies of the same comparison, the risk differences were pooled by use of a random effects model. A two-tailed P value, pertaining to the pooled risk difference, was derived from this procedure. The Q statistic was used to test for homogeneity of effect sizes. If the Q statistic for the primary objective of the meta-analysis, that is, comparison of initial eradication rates, revealed significant heterogeneity ($P<0.05$), meta-analysis was not used. A normal approximation (Z) test (two-tailed) was used to evaluate the statistical significance of risk differences for individual studies.

METHODS USED TO FORMULATE THE RECOMMENDATIONS

Not stated

RATING SCHEME FOR THE STRENGTH OF THE RECOMMENDATIONS

Strength of recommendation:

A. Good evidence to support a recommendation for use
B. Moderate evidence to support a recommendation for use
C. Poor evidence to support a recommendation
D. Moderate evidence to support a recommendation against use
E. Good evidence to support a recommendation against use

COST ANALYSIS

A formal cost analysis was not performed and published cost analyses were not reviewed.

METHOD OF GUIDELINE VALIDATION

External Peer Review
Internal Peer Review

DESCRIPTION OF METHOD OF GUIDELINE VALIDATION

The document has been subjected to external review by peer reviewers as well as by the Practice Guidelines Committee and was approved by the Infectious Diseases Society of America Council.

A prepublication draft was circulated to 27 selected experts in the urinary tract infection field, and 26 returned comments, some of which were incorporated in subsequent manuscript revisions.

RECOMMENDATIONS

MAJOR RECOMMENDATIONS

Excerpted by the National Guideline Clearinghouse (NGC)

Each recommendation includes a ranking for the strength and the quality of evidence supporting it. Definitions of the levels of evidence (I-III) and grades of recommendation (A-E) are repeated at the end of the Major Recommendations field.

Acute Uncomplicated Bacterial Cystitis

In otherwise healthy adult nonpregnant women with acute uncomplicated bacterial cystitis, single-dose therapy is generally less effective than the same antimicrobial used for longer durations (AI). However, most antimicrobials given for 3 days are as effective as the same antimicrobial given for a longer duration (AI).

Trimethoprim-sulfamethoxazole for 3 days should be considered the current standard therapy (AI). Trimethoprim alone (AII) and ofloxacin (AI) are equivalent to trimethoprim-sulfamethoxazole; other fluoroquinolones, such as norfloxacin, ciprofloxacin, and fleroxacin, are probably of similar effectiveness (AII). Fluoroquinolones are more expensive than trimethoprim-sulfamethoxazole and trimethoprim, and, to postpone emergence of resistance to these drugs, we do not recommend them as initial empirical therapy except in communities with high rates of resistance (i.e., >10%–20%) to trimethoprim-sulfamethoxazole or trimethoprim among uropathogens. When given for 3 days, beta-lactams as a group are less effective than the foregoing drugs (EI). Nitrofurantoin and fosfomycin may become more useful as resistance to trimethoprim-sulfamethoxazole and trimethoprim increase (BI).

Acute pyelonephritis. The few properly designed trials for management of acute pyelonephritis are several years old, precluding recommendations firmly based on recent evidence. For young nonpregnant women with normal urinary tracts presenting with an episode of acute pyelonephritis, 14 days of antimicrobial therapy is appropriate (AI); courses of highly active agents as short as 7 days may be sufficient for mild or moderate cases (BI). Mild cases can be managed with oral medications (AII), and we recommend an oral fluoroquinolone (AII) or, if the organism is known to be susceptible, trimethoprim-sulfamethoxazole (BII). If a gram-positive bacterium is the likely causative organism, amoxicillin or amoxicillin/clavulanic acid may be used alone (BIII). Patients with more severe cases of acute pyelonephritis should be hospitalized (AII) and treated with a

parenteral fluoroquinolone, an aminoglycoside with or without ampicillin, or an extended-spectrum cephalosporin with or without an aminoglycoside (BIII); if gram-positive cocci are causative, we recommend ampicillin/sulbactam with or without an aminoglycoside as therapy (BIII). With improvement, the patient´s regimen can be changed to an oral antimicrobial to which the organism is susceptible to complete the course of therapy (BIII).

Definitions of Strength of Recommendation and Quality of Evidence Ratings:

Quality of evidence:

I. Evidence from at least one properly randomized, controlled trial
II. Evidence from at least one well-designed clinical trial without randomization, from cohort or case-control analytic studies (preferably from more than one center), from multiple time-series studies, or from dramatic results of uncontrolled experiments
III. Evidence from opinions of respected authorities based on clinical experience, descriptive studies, or reports of expert committees

Strength of recommendation:

A. Good evidence to support a recommendation for use
B. Moderate evidence to support a recommendation for use
C. Poor evidence to support a recommendation
D. Moderate evidence to support a recommendation against use
E. Good evidence to support a recommendation against use

CLINICAL ALGORITHM(S)

None provided

EVIDENCE SUPPORTING THE RECOMMENDATIONS

TYPE OF EVIDENCE SUPPORTING THE RECOMMENDATIONS

The type of supporting evidence is identified and graded for each recommendation (see "Major Recommendations").

BENEFITS/HARMS OF IMPLEMENTING THE GUIDELINE RECOMMENDATIONS

POTENTIAL BENEFITS

Symptomatic urinary tract infections are among the most common of bacterial infections. A variety of antimicrobial regimens comprising different drugs, doses, schedules, and durations have been used to treat urinary tract infections. Information on diagnosis and treatment of urinary tract infections can assist primary care providers in dispensing the proper treatment thereby resulting in resolution of symptoms and limiting potential microbial resistance.

POTENTIAL HARMS

Adverse effects associated with antimicrobial drugs, such as side effects and drug resistance.

QUALIFYING STATEMENTS

QUALIFYING STATEMENTS

These guidelines are based on antimicrobial susceptibilities reported in the late 1990s, which are changing over time and vary geographically; thus, we recommend that communities periodically reassess susceptibility of uropathogens to commonly used antibiotics.

Recommendations regarding the treatment of acute pyelonephritis are limited by the relative paucity of appropriate studies. Controlled trials examining management of acute pyelonephritis are few, and many of the available studies are weakened by participation of heterogeneous populations, including men and patients with complicated urinary tracts.

IMPLEMENTATION OF THE GUIDELINE

DESCRIPTION OF IMPLEMENTATION STRATEGY

Performance measures are provided to aid in monitoring compliance with the guideline.

Indications and Performance Measures

Uncomplicated acute bacterial cystitis in women
The indicator, in areas where the prevalence of resistance to trimethoprim-sulfamethoxazole and to trimethoprim is less than 20%, is that uncomplicated acute bacterial cystitis should be treated for 3 days with trimethoprim-sulfamethoxazole or trimethoprim. The performance measure would be the rate of compliance with this A,I recommendation. The denominator would be all, otherwise healthy, adult nonpregnant women with symptoms of frequency, urgency, and/or dysuria and with greater than or equal to 102 cfu of bacteria/mL of urine. The numerator would be the number of such women treated with oral trimethoprim sulfamethoxazole or trimethoprim for 3 days.

Uncomplicated acute pyelonephritis in women
The indicator is that otherwise healthy young women with acute pyelonephritis should be treated for 7–14 days, mostly with oral antibiotics. The performance measure would be degree of compliance with this B,I recommendation. The denominator would be all, young, otherwise healthy, nonpregnant women with normal urinary tracts presenting with flank pain and/or fever and with greater than or equal to 102 cfu of bacteria/mL of urine. The numerator would be the number of such women treated for 7–14 days, either totally with oral antibiotics or with oral antibiotics following improvement with initial parenteral antibiotics.

INSTITUTE OF MEDICINE (IOM) NATIONAL HEALTHCARE QUALITY REPORT CATEGORIES

IOM CARE NEED

Getting Better

IOM DOMAIN

Effectiveness

IDENTIFYING INFORMATION AND AVAILABILITY

BIBLIOGRAPHIC SOURCE(S)

Warren JW, Abrutyn E, Hebel JR, Johnson JR, Schaeffer AJ, Stamm WE. Guidelines for antimicrobial treatment of uncomplicated acute bacterial cystitis and acute pyelonephritis in women. Infectious Diseases Society of America (IDSA). Clin Infect Dis 1999 Oct;29(4):745-58. [82 references]

ADAPTATION

Not applicable: The guideline was not adapted from another source.

DATE RELEASED

1999 Oct

GUIDELINE DEVELOPER(S)

Infectious Diseases Society of America - Medical Specialty Society

SOURCE(S) OF FUNDING

Infectious Diseases Society of America (IDSA)

GUIDELINE COMMITTEE

Infectious Diseases Society of America (IDSA) Practice Guidelines Committee

COMPOSITION OF GROUP THAT AUTHORED THE GUIDELINE

Authors: John W. Warren, Elias Abrutyn, J. Richard Hebel, James R. Johnson, Anthony J. Schaeffer, and Walter E. Stamm.

FINANCIAL DISCLOSURES/CONFLICTS OF INTEREST

Not stated

GUIDELINE STATUS

This is the current release of the guideline.

An update is not in progress at this time.

GUIDELINE AVAILABILITY

Electronic copies: Available in Portable Document Format (PDF) from the Infectious Diseases Society of America (IDSA) Web site.

Print copies: Available from the University of Chicago Press; fax: (773) 702-6096.

AVAILABILITY OF COMPANION DOCUMENTS

The following are available:

- Kish MA. Guide to development of practice guidelines. Clinical Infectious Diseases 2001;32:851-4.
- Gross PA. Practice guidelines for infectious diseases: Rationale for a work in progress. Clin Infect Dis. 1998 May;26(5):1037-41.
- Gross PA, Barrett TL, Dellinger EP, Krause PJ, Martone WJ, McGowan JE Jr, Sweet RL, Wenzel RP. Purpose of quality standards for infectious diseases. Infectious Diseases Society of America. Clin Infect Dis 1994 Mar;18(3):421.

Electronic copies: Available from the Infectious Diseases Society of American (IDSA) Web site.

Print copies: Available from Infectious Diseases Society of America, 66 Canal Center Plaza, Suite 600, Alexandria, VA 22314.

PATIENT RESOURCES

None available

NGC STATUS

This summary was completed by ECRI on May 1, 2001. The information was verified by the guideline developer as of June 29, 2001.

COPYRIGHT STATEMENT

Date Modified: 11/8/2004